renal hypouricemia

Renal hypouricemia is a kidney (renal) disorder that results in a reduced amount of uric acid in the blood. Uric acid is a byproduct of certain normal chemical reactions in the body. In the bloodstream it acts as an antioxidant, protecting cells from the damaging effects of unstable molecules called free radicals. However, having too much uric acid in the body is toxic, so excess uric acid is removed from the body in urine.

People with renal hypouricemia have little to no uric acid in their blood; they release an excessive amount of it in the urine. In many affected individuals, renal hypouricemia causes no signs or symptoms. However, some people with this condition develop kidney problems. After strenuous exercise, they can develop exercise-induced acute kidney injury, which causes pain in their sides and lower back as well as nausea and vomiting that can last several hours.

Because an excessive amount of uric acid passes through the kidneys to be excreted in urine in people with renal hypouricemia, they have an increased risk of developing kidney stones (nephrolithiasis) formed from uric acid crystals. These uric acid stones can damage the kidneys and lead to episodes of blood in the urine (hematuria). Rarely, people with renal hypouricemia develop life-threatening kidney failure.

Frequency

The prevalence of renal hypouricemia is unknown; at least 150 affected individuals have been described in the scientific literature. This condition is thought to be most prevalent in Asian countries such as Japan and South Korea, although affected individuals have been found in Europe. Renal hypouricemia is likely underdiagnosed because it does not cause any symptoms in many affected individuals.

Genetic Changes

Mutations in the *SLC22A12* or *SLC2A9* gene cause renal hypouricemia. These genes provide instructions for making proteins called urate transporter 1 (URAT1) and glucose transporter 9 (GLUT9), respectively. These proteins are found in the kidneys, specifically in structures called proximal tubules. These structures help to reabsorb needed nutrients, water, and other materials into the blood and excrete unneeded substances into the urine. Within the proximal tubules, both the URAT1 and GLUT9 proteins reabsorb uric acid into the bloodstream or release it into the urine, depending on the body's needs. Most uric acid that is filtered through the kidneys is reabsorbed into the bloodstream; about 10 percent is released into urine.

Mutations that cause renal hypouricemia lead to the production of URAT1 or GLUT9 protein with a reduced ability to reabsorb uric acid into the bloodstream. Instead, large

amounts of uric acid are released in the urine. The specific cause of the signs and symptoms of renal hypouricemia is unclear. Researchers suspect that when additional uric acid is produced during exercise and passed through the kidneys, it could lead to tissue damage. Alternatively, without the antioxidant properties of uric acid, free radicals could cause tissue damage in the kidneys. Another possibility is that other substances are prevented from being reabsorbed along with uric acid; accumulation of these substances in the kidneys could cause tissue damage. It is likely that individuals with renal hypouricemia who have mild or no symptoms have enough protein function to reabsorb a sufficient amount of uric acid into the bloodstream to prevent severe kidney problems.

Inheritance Pattern

This condition is typically inherited in an autosomal recessive pattern, which means both copies of the *SLC22A12* or *SLC2A9* gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they usually do not show signs and symptoms of the condition.

Sometimes, individuals with one *SLC2A9* gene mutation in each cell have reduced levels of uric acid. The levels usually are not as low as they are in people who have mutations in both copies of the gene, and they often do not cause any signs or symptoms. Rarely, people who carry one copy of the mutated gene will develop uric acid kidney stones.

Other Names for This Condition

- familial renal hypouricaemia
- familial renal hypouricemia
- hereditary renal hypouricemia
- RHUC

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: Familial renal hypouricemia
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0473219/
- Genetic Testing Registry: Renal hypouricemia 2
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C2677549/

Other Diagnosis and Management Resources

- KidsHealth from Nemours: Blood Test: Uric Acid
  http://kidshealth.org/en/parents/test-uric.html
- MedlinePlus Encyclopedia: Uric Acid--Blood
  https://medlineplus.gov/ency/article/003476.htm

General Information from MedlinePlus

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html
- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html
- Palliative Care
  https://medlineplus.gov/palliativecare.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html

Additional Information & Resources

MedlinePlus

- Encyclopedia: Acute Kidney Failure
  https://medlineplus.gov/ency/article/000501.htm
- Encyclopedia: Acute Tubular Necrosis
  https://medlineplus.gov/ency/article/000512.htm
- Encyclopedia: Uric Acid--Blood
  https://medlineplus.gov/ency/article/003476.htm
- Health Topic: Kidney Diseases
  https://medlineplus.gov/kidneydiseases.html

Genetic and Rare Diseases Information Center

- Renal hypouricemia
  https://rarediseases.info.nih.gov/diseases/9496/renal-hypouricemia

Additional NIH Resources

- National Institute of Diabetes and Digestive and Kidney Diseases: Hematuria (Blood in the Urine)
  https://www.niddk.nih.gov/health-information/urologic-diseases/hematuria-blood-urine
- National Institute of Diabetes and Digestive and Kidney Diseases: What I Need to Know About Kidney Stones
  https://www.niddk.nih.gov/health-information/urologic-diseases/kidney-stones

Educational Resources

- Disease InfoSearch: Familial renal hypouricemia
  http://www.diseaseinfosearch.org/Familial+renal+hypouricemia/8406
- National Health Service (NHS) (UK): Causes of Kidney Stones
  http://www.nhs.uk/Conditions/Kidney-stones/Pages/Causes.aspx
- National Kidney Foundation: Acute Kidney Injury
  https://www.kidney.org/atoz/content/AcuteKidneyInjury
- Orphanet: Hereditary renal hypouricemia
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=94088

Patient Support and Advocacy Resources

- American Kidney Fund: Acute Kidney Injury
  http://www.kidneyfund.org/kidney-disease/kidney-problems/acute-kidney-injury.html
- National Kidney Foundation
  https://www.kidney.org/

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28renal+hypouricemia%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D

OMIM

- HYPOURICEMIA, RENAL, 1
  http://omim.org/entry/220150
- HYPOURICEMIA, RENAL, 2
  http://omim.org/entry/612076

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Reprinted from Genetics Home Reference:
https://ghr.nlm.nih.gov/condition/renal-hypouricemia

Reviewed: January 2015
Published: March 21, 2017

Lister Hill National Center for Biomedical Communications
U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services